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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,483	01/10/2001	Yoshiyuki Matsumoto	Q62437	2611

7590

04/14/2004

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2100 Pennsylvania Avenue NW Suite 800  
Washington, DC 20037-3213

EXAMINER
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HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/743,483	MATSUMOTO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Evelyn Huang	1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 18-30 and 35-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18-30 and 35-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12-29-2003 has been entered.

### ***Claim Rejections - 35 USC § 112***

2. The rejection for Claims 23, 29 under 35 U.S.C. 112, second paragraph, is withdrawn because the amendment has obviated the rejection.

### ***Duplicate Claims***

3. The cancellation of claim 31 has rendered moot the objection to its being a substantial duplicate of claim 30.

### ***Claim Rejections - 35 USC § 103***

4. The rejection for Claims 18-22, 26-29 under 35 U.S.C. 103(a) as being unpatentable over Shimamura (JP 05112559) is withdrawn in view of the amendment limiting J to the recited ring moieties when  $m=0$  and A is a ring system, thereby setting a demarcation from Shimamura's compound which has an alkyl group. Motivation to modify Shimamura's compound to arrive at the instant invention is lacking.

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***Double Patenting***

5. The provisional obviousness-type double patenting over corresponding claims of copending Application No. 09/936566 is maintained for reasons of record. Applicant has requested the examiner to hold this rejection in abeyance until allowable subject matter is indicated in this application or in the co-pending application. A timely filed terminal disclaimer would obviate the rejection.

6. The provisional obviousness-type double patenting as being unpatentable over corresponding claims of copending Application No. 10/169866 is maintained for reasons of record. Applicant has requested the examiner to hold this rejection in abeyance until allowable subject matter is indicated in this application or in the co-pending application. A timely filed terminal disclaimer would obviate the rejection.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The mechanism of inhibiting chymase reaches out to as yet unidentified conditions associated therewith.

***Claim Rejections - 35 USC § 112***

8. The 35 U.S.C. 112, first paragraph rejection set forth in the office action mailed on 11-14-2002 is replaced with the following 112 first paragraph rejection.

Claims 35-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification is only enabling for using the inventive compounds for treatment of cardiovascular diseases such as cardiac failure or arthritis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

a. *Nature of the invention.*

The instant invention is drawn to a thiobenzimidazo compound for inhibition of chymase, and for treatment or prevention of diseases recited on page 1 of the specification

b. *State of the prior art and the level of the skill in the art.*

A heterocyclic amide compound has been shown to inhibit chymase (Akahoshi, WO 98/18794, or 6080738, its US equivalent). A thiobenzimidazole compound similar to the instant has been shown to be an antagonist of the thromboxane receptor by Bru-Magniez I (5021443, PTO-1449), Bru-Magniez II (5124336, PTO-1449) and Bru-Magniez III (51228359, PTO-1449) or gastric acid secretion inhibitor (JP 62212386, PTO-1449; JP 1-265089, PTO-1449).

While chymase may be implicated in various diseases, at the time of the invention, the pathophysiological roles of chymase has not been clarified (Nakayama et al. Nippon rinsho. Japanese Journal of Clinical Medicine. 1997, 55(8):1903-8, abstract). It has recently been shown that chymase positive mast cells have no relation to clinical manifestation of atopic disease or asthma (Saarinen et al. Allergy, 2001, 56(1):58-64, abstract).

The skill in the chymase inhibitor art is high.

c. *Predictability/unpredictability in the art.*

The high degree of unpredictability is well recognized in the chymase inhibitor art. A slight modification of the compound would lead to profound changes in its biological activity as evidenced in the very different  $K_i$  values for human heart chymase exhibited by structurally similar compounds (Akahoshi, Table 10 ).

d. *Amount of guidance/working examples.*

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The procedure for the measurement of human mast cell chymase and the results thereof are described on page 90 of the specification, however, no in vivo functional assays are shown.

e. *The breadth of the claims.*

Applicant's assertion that all the inventive compounds would be effective in treating all the diseases recited in the specification does not commensurate with that of the objective enablement, especially in view of that at the time of the invention, the pathophysiological roles of chymase has not been clarified, the high degree of unpredictability in the art and the limited working examples (paragraphs c, d above).

f. Amount of undue experimentation. Since insufficient teaching and guidance are provided by the specification (paragraphs c-d above), one of ordinary skill in the art, even with high degree of skill, would not be able to use all the compounds as claimed without undue experimentation, especially when the nexus between inhibition of chymase and the treatment of these recited diseases has not been fully established.

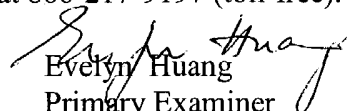
***Allowable Subject Matter***

9. Claims 18-30 would be allowed if the obviousness type double patenting were overcome. See paragraph 4 above.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Evelyn Huang  
Primary Examiner  
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